NOT FOR PUBLICATION WITHOUT THE APPROVAL OF THE COMMITTEE ON OPINIONS

SUPERIOR COURT OF NEW JERSEY

COUNTIES OF
ATLANTIC AND CAPE MAY

CAROL E. HIGBEE, P.J.Cv.

1201 Bacharach Boulevard
Atlantic City, NJ 08401-4527
(609) 343-2190

MEMORANDUM OF DECISION ON MOTION
Pursuant to Rule 1:6-2(f)

CASE:	**McCarrell v. Hoffmann-LaRoche Inc.**
DOCKET #:	**ATL-L-1951-03-MT**
DATE:	**February 8, 2008**
MOTION:	**Defendant's Motion for JNOV**
ATTORNEYS:	**Diane E. Lifton – Defendant** **David R. Buchanan - Plaintiff**

Having carefully reviewed the papers submitted and any response filed, I have ruled on the above Motion as follows:

Following a three week trial, in which plaintiff Andrew McCarrell was awarded just over $2.5 million dollars in damages for injuries sustained stemming from his use of the drug Accutane manufactured by defendants Hoffman-La Roche, Inc. and Roche Laboratories, Inc. (hereinafter "Roche"), defendants brought this motion for a judgment notwithstanding the verdict or, in the alternative, a new trial.

Background

Plaintiff began taking Accutane in order to treat acne in June 1995 and continued taking it through October of that year. In the year following his course of Accutane treatment plaintiff

experienced symptoms including abdominal pain, diarrhea, and rectal bleeding. On November 26, 1996, plaintiff was diagnosed with Inflammatory Bowel Disease ("IBD").[1] Plaintiff was first treated with antibiotics, followed by a course of steroids, and eventually underwent surgery to remove his colon. In the years following the colectomy plaintiff suffered from a host of complications from the colon removal and endured subsequent surgery. Plaintiff then brought suit against defendants arguing that Accutane was the cause of his IBD and that defendants failed to adequately warn his treating physician of the risks of IBD from Accutane.

Applicable Law

A judgment notwithstanding the verdict is given only if "upon accepting as true all the evidence that supports the opponent's position, and upon providing the opponent with all reasonable inferences, reasonable minds could not differ." Sun Coast Merchandise Corp. v. Myron Corp., 393 N.J. Super. 55, 70 (App. Div. 2007). This standard has been interpreted to require "the evidence and uncontradicted testimony [to be] plain and so complete that disbelief of the story could not reasonably arise in the rational process of an ordinary intelligent mind." Id. citing Ferdinand v. Agricultural Ins. Co., 22 N.J. 482, 494 (1956) (internal quotations omitted).

The Court shall grant a new trial only if "having given due regard to the opportunity of the jury to pass upon the credibility of the witnesses, it **clearly and convincingly** appears that there was a miscarriage of justice under the law." N.J. R. 4:49-1(a) (emphasis added). Further, "[j]ury verdicts should be set aside in favor of new trials only with great reluctance, and only in cases of clear injustice." Boryszewski v. Burke, 380 N.J. Super. 361, 391 (App. Div. 2005), certif. den. 186 N.J. 242 (2006).

[1] IBD encompasses two diseases, Crohn's Disease and ulcerative colitis. Plaintiff was diagnosed with the latter form of IBD which causes inflammation and damage to the lining of the colon. Trial Tr. at 801:24-802:15.

Defendants argue that they were harmed at trial by improper use of the internal Roche documents known as "causality assessments," plaintiff's arguments that Roche failed to adequately test Accutane, and the Court's exclusion of certain defense evidence. Defendants further argue that the evidence did not support the verdict and that the trial was tainted by prejudicial evidence and misconduct of plaintiff's counsel. The Court will address these arguments *seriatim*.

Admission of Dr. Sachar's Opinion on Causality

First the Court must address the defense argument that Dr. Sachar's opinion on causation should have been stricken. The defendants rely heavily on the decision of Hon. James Moody, District Judge, U. S. District Court Middle District of Florida, to support the argument that the plaintiff's expert, Dr. Sachar, did not have a scientific basis for his opinion on general causation. Judge Moody made his decisions based on the evidence, arguments, and law before him. The expert used by plaintiff's counsel in New Jersey was not the same expert offered in the Federal Court. The decision made by Judge Moody does not reflect consideration of significant parts of the testimony and evidence placed before this Court. Further, as it was a federal district Court sitting in Florida, it is not binding precedent. It is clear that Judge Moody did not have the same evidence before him as was presented in this Court.

The New Jersey Supreme Court has set forth the legal principles governing a trial judge's decision as to whether to admit the opinion of an expert on causation in a complex and evolving scientific world. First, it must be recognized that science and law are two very different disciplines. Scientists are always in the process of questioning, testing, and evaluating. Because science is based on creating a hypothesis or a theory and trying to prove or disprove it they are trained not to accept anything as final. Scientists constantly rethink and challenge accepted

theories. In a lawsuit, however, a particular plaintiff has to prove that a particular fact, such as medical causation, is more likely than not based on the evidence presented at that moment. It is no wonder that presentation of scientific opinions in a legal setting has been the subject of shifting legal doctrines. The Court must prevent juries from being presented with evidence that has no scientific reliability and is in fact is "junk science" by "experts" who are basically giving a personal opinion that is not reliable. There are people in every field who will espouse bizarre opinions for which there is no reliable evidence if paid enough. Courts cannot allow these types of "expert opinions" if there exists no reliable evidence to support them.

The Court's gatekeeping role, however, is not to decide if the expert's opinion is right or wrong, but to determine if there is sufficient reliability to the opinion to allow the expert to give it. See Landrigan v. Celotex, 127 N.J. 404, 414. The old New Jersey legal standard under Frye v. United States, 293 F. 1013, was to determine if the expert's opinion was generally accepted by a portion of the scientific community. However, in 1991 and 1992, the New Jersey Supreme Court recognized that the scientific community's standard for acceptance of something as proven is different than a legal standard. Justice Handler, writing for a unanimous Court, stated:

> We recognize, too, that because of the extremely high level of proof required before scientists will accept a new theory, and particularly because of the current inability of science to fully comprehend carcinogenesis, *see Brennan, Causal Chains and Statistical Links: The Role of Scientific Uncertainty in Hazardous-Substance Litigation, 73 Cornell L.Rev.469, 474-75(1988),* plaintiffs in toxic-tort litigation, despite strong and indeed compelling indicators that they have been tortiously harmed by toxic exposure, may never recover if required to await general acceptance by the scientific community of a reasonable, but as yet not certain, theory of causation. Rubanick v. Witco Chemical Corp., 125 N.J. 421, 433.

The present standard in New Jersey is that set forth in Rubanick:

> [A] scientific theory of causation that has not yet reached general acceptance may be found to be sufficiently reliable if it is based on a sound, adequately-founded scientific methodology involving data and information of the type

> reasonably relied on by experts in the scientific field. The evidence of such scientific knowledge must be proffered by an expert who is sufficiently qualified by education, knowledge, training, and experience in the specific field of science. The expert must possess a demonstrated professional capability to assess the scientific significance of the underlying data and information, to apply the scientific methodology, and to explain the bases for the opinion reached.

With that standard in mind the Court evaluated Dr. Sachar's testimony. The proper question before this Court is whether under New Jersey law, based on the evidence presented here, was plaintiff's expert Dr. Sachar's opinion on causation admissible or should it have been excluded? First, this Court looked at the qualifications of Dr. Sachar to render an opinion. His qualifications were very impressive; Dr. Sachar has studied, practiced, taught and published extensively. In fact, the testimony on his qualifications was so lengthy because of the level of his accomplishments in the field of gastroenterology, this Court eventually asked counsel to move out of the area of qualifications in the interest of time. It is clear that he is one of the most respected gastroenterologists in the country.

When evaluating the reliability of an expert's opinion the fact that the expert is one of the most experienced and respected persons in his field certainly should be given some consideration. This Court found that the fact that a highly qualified gastroenterologist holds the opinion that Accutane ingestion can be a significant contributing factor in causing IBD, a gastrointestinal disease, is something that should be considered when deciding whether the jury should hear that opinion.

Of course, having good qualifications alone are not enough. The expert must have the ability to explain his opinion and the scientific principles upon which he relied in reaching his opinion. In addition, he must rely on data and studies using a methodology that is supported by some expert consensus in the appropriate field.

Dr. Sachar acknowledged that IBD is described as idiopathic because the etiology is unknown. That is, the exact cause of IBD is not fully understood by the scientific community. He was completely candid about this fact. This is true of causation in many conditions and diseases. For example, the etiology of lung cancer is not fully understood, yet the fact that smoking tobacco substantially increases the risk of lung cancer is accepted by most of the scientific community. The exact cause of heart attacks is much less understood than generally believed by lay persons, but the fact that smoking increases the risk of heart attack is also accepted as true by the scientific community.

IBD, whether Chron's Disease, as the plaintiff had here, or ulcerative colitis is a disease of the intestines. Dr. Sachar explained, based on his extensive experience treating and researching, that there was a biologically, plausible mechanism for his opinion. In other words, it makes sense based on what is known about the way the body works. If there is a biologically, plausible explanation for why one thing would affect another, then it is more inherently reliable than if there is no biologically, plausible mechanism. See Landrigan v. Celotex, 127 N.J. 404 (discussing biological correlations that lack a plausible mechanism versus those that have a plausible mechanism).

Dr. Sachar testified that it is known that the intestines have a mucosal lining and that the mucosal lining of epidermal cells serves as a protective barrier to the intestine. He noted that Accutane cures acne so it is clear it affects the epidural layer of cells of the skin where acne occurs. He also noted it is known that Accutane acts as a drying agent causing, for example, chapped lips and dry skin are known common side effects. Since the intestines are lined and protected by a mucosal lining of epidural cells, Dr. Sachar testified that it is biologically plausible that Accutane would disrupt the mucosal lining of the intestines and allow damage to

the intestine. IBD is described, at times, as a disease of the mucosa of the intestines. Again, defendants argue Dr. Sachar can't opine exactly how Accutane cures acne or how it causes IBD, but he did offer a plausible biological mechanism as to why Accutane would be a substantial factor in causing IBD.

Animal Studies

Dr. Sachar's expert opinion relied on several factors, including his review of numerous animal studies conducted by the defendants on dogs. Judge Moody details one of the dog studies and finds it lacks scientific reliability because of questions about dosage. While animal studies can have significant limitations, they are generally considered scientific studies and are accepted and relied upon by the scientific community. The limitations of animal studies can be tested on cross-examination, but a properly conducted animal study on a drug is an accepted scientific method. They are used extensively by drug manufacturers and scientists and are relied on by both in making decisions and forming opinions. Here, the studies used by Dr. Sachar were conducted by the defendant.

The two drawbacks of animal studies are first, that they are done on animals and the results have to be extrapolated to predict a result on humans, and second, animal testing usually uses larger doses of drugs than are used on humans. These limitations don't make the methodology unscientific. They do affect the weight to be given and animal studies alone would usually not be enough to give an opinion on causation. However, the scientific community, including the FDA and the scientists at Hoffmann-LaRoche, clearly believe there is important scientific information to be gained from animal studies. The FDA requires them to evaluate new drugs before approval.

There was a scientific purpose to these studies and it was obviously to investigate the effects of the drugs on a species similar enough to humans that the results would matter. Dr. Sachar testified that he relied on not one, but multiple dog studies in informing his opinion. One of the advantages to dog studies is that the animal can be and usually is autopsied at the end of the study and the scientists can look at the animal tissue after the drug has been administered, which cannot be done on humans for obvious reasons. This is an accepted scientific method to evaluate the effects of a drug. It is not conclusive proof of cause and effect, but it is the type of information scientists rely on in forming an opinion.

Dr. Sachar testified about study Ro 4-3780, which was a fifty-five week Accutane study conducted by Roche on dogs. He read to the jury statements made by Roche scientists in their own report on the findings *based on inspection of tissue during autopsy*. The report Dr. Sachar read stated:

> "[A] variety of gross anatomic changes were observed in the gastrointestinal tract at autopsy, and their nature is suggestive of gastrointestinal irritation, the frequency with which these changes were observed is clearly dose-related, they were observed in the mid and low-dose groups only in dogs sacrificed at the end of the study, but were observed in some high dose dogs sacrificed at 30 weeks. These findings and the relatively high incidence of gastrointestinal bleeding in treated dogs suggest that treatment with Ro 4-370 is associated with gastrointestinal irritation." Trial Tr. of May 9, 2007 at 840:10-21.

This language came from a report of Roche's own scientists based on a properly executed scientific study of dogs. This is accepted scientific methodology looking at reports of scientists who examined tissue from the test animals. The test alone doesn't prove that Accutane causes IBD, but the results do help support his opinion.

The Roche report itself stated that both low and mid-dose groups of dogs showed gastrointestinal irritation when sacrificed at the end of the study. Dr. Sachar discussed with the jury the dose related issues on direct examination. He also discussed other dog studies showing

visible blood, diarrhea, visible bloody mucous, etc. He testified on direct that he looked at a lot of the animal studies because some involved megadosing, but others were "at doses and at concentrations that were actually achieved in human therapy... ." Trial Tr. 849:1-3. In reading from the reports of the studies, Dr. Sachar noted reports showing "focal gross anatomic lesions" in the intestines. Trial Tr. 841:16.

The weaknesses of animal studies were discussed by Dr. Sachar himself, and he was cross-examined at length by Roche's skillful counsel. Dr. Sachar testified on direct, and acknowledged in cross-examination, that some of the animals used large doses of the drug. He testified large doses are used to determine what kinds of adverse effect might occur in humans even at normal doses. Trial Tr. 1057:19-25, 1058:1-9. On cross examination he testified again that some of the animal studies that were significant to him had concentrations of the drug that mimic those used in humans. Trial Tr. 1060:6-10. Despite the opportunity, the defense counsel did not challenge Dr. Sachar's statements that some of the animal studies he relied upon used doses that mimic human doses.

The Court allowed, over strenuous objections by plaintiffs, the defense to cross-examine Dr. Sachar with a seventy-five person human study conducted with approximately twenty-five people in three groups, in an attempt to impeach Dr. Sachar's testimony about results in one of the dog studies. However, the defense asked minimal questions after being allowed to use the study. Dr. Sachar on redirect testified that in the human study at least 10% of the human subjects had levels of a metabolite of Accutane 4-oxo-istobetinoin in their blood that were at or above the level that consistently produced bloody diarrhea in the dogs. Trial Tr. 123:12-15, 1234:1-3.

This Court finds that the animal studies were admissible. No scientific study is perfect, but these studies were relevant, could support the expert's opinion, and were done using an

accepted scientific methodology. Further, they were of a type commonly relied upon by the scientific community, and the weaknesses in the studies were, of course, subjected to cross-examination.

Other Evidence Relied Upon by Dr. Sachar

Dr. Sachar also relied upon and testified about reports by physicians that described challenge/dechallenge/rechallenge events. A doctor that reports on challenge/dechallenge/ rechallenge is describing something more than just an event that occurred while on a drug. If the doctor puts the patient on a drug and the patient develops an adverse condition or symptom and the doctor takes the patient off the drug and the symptom goes away, that is a challenge/dechallenge finding. If the doctor puts the patient back on the drug and the patient develops the symptom again, that is a positive rechallenge. Dr. Sachar testified this type of challenge/dechallenge/rechallenge report is considered very significant to scientists based on his experience as chairman of an FDA advisory committee. Trial Tr. 897:1-13. Dr. Sachar testified that he reviewed Roche's files containing these challenge/dechallenge and positive rechallenge reports involving Accutane and IBD.

Dr. Sachar relied upon over a dozen of these case reports where the patient had symptoms of IBD on Accutane, was removed from the drug and the symptoms stopped, and then placed back on the drug and symptoms reoccurred. The defense cross-examined him about the fact that the nature of IBD is that symptoms may go into remission and then reappear. Again, this is not a basis to bar the evidence only a weakness that can be examined on cross-examination. Challenge/dechallenge/rechallenge is a scientific testing mechanism used and accepted by the medical and scientific community. A scan of medical literature will demonstrate that scientists

use this method to evaluate causal links between a drug and an adverse effect. Again, this is just one other piece of evidence that Dr. Sachar testified that he relied upon in his opinion.

In addition to the reports in Roche's files, Dr. Sachar relied upon published medical literature in peer reviewed journals to support his opinion. He testified about an article called "Isotretinoin-Associated Proctosigmoiditis." This was a case report published in the official journal of the American Gastroenterology Association. The article describes a challenge/dechallenge/positive rechallenge involving Accutane and inflammatory bowel disease. Isotretinoin is Accutane. The article stated:

> "Although the pathogenesis of the colonic mucosal inflammation remains unknown, the relationships of the bouts of proctosigmoiditis to the administration of Isotretinoin strongly suggests that the drug was directly responsible."
> Trial Tr. 963:18-22

The language discrepancy between that used by the scientific/medical community and the law was explained by Dr. Sachar as follows:

> "Now, the term they use here is 'strongly suggests.' That's the most a medical report ever says. It is the vocabulary of published biomedical reports. It is the custom. It is the tradition never to say 'proves' or 'shows' or 'demonstrates.' That's taboo. You just don't say that in publication.
> So, what one says in polite scientific published conversation, you always say 'suggests,' and if you really want to say it is the real thing, you say 'strongly suggests.' That's as strong as anybody ever gets in print."
> Trial Tr. 964:10-20.

In addition, Dr. Sachar testified about two other peer reviewed articles that discussed IBD and Accutane from peer reviewed journals. The Court did not allow the expert to rely on a physician review manual that was not peer reviewed. Dr. Sachar further noted in his testimony that the "Yamada" textbook is the premier textbook on gastroenterology and read from it as follows:

> "A. It says that isotretinoin has been linked to acute colitis and to the reactivation of quiescent inflammatory bowel disease.

Q. Does it also reference the rechallenge?

A. Yes, it references one of the same references that we have already discussed." Trial Tr. 991:13-18.

The Reddy Article

Dr. Sachar also relied upon The Reddy Article, a peer reviewed article published in the American Journal of Gastroenterology 2006, 101:1569-1573. This article described a study by scientists/doctors on the question of whether Accutane causes IBD. The title of the article is "Possible Association Between Isotretinoin and Inflammatory Bowel Disease." The authors are Dr. Deepa Reddy and Dr. Sunanda Kane from the University of Chicago and Dr. Corey Siegel and Dr. Bruce Sands from Massachusetts General/Harvard medical School. This was a study done by these outside researchers. They reviewed every MedWatch report filed with the FDA and then "applied a validated tool to assess causality."

The two groups of doctors from University of Chicago and Massachusetts General Hospital obtained the MedWatch reports from the FDA and from Roche's database. Each group independently reviewed and collected data from all the reports including data on sex and age of patient, date of onset of symptoms, dates of usage, dosage, diagnostic information, pertinent history, ultimate outcome, and dechallenge or rechallenge on the drug.

After this review, the two sets of scientists assembled the cases and used the Naranjo probability score to assess the causal relationship between IBD and use of Accutane. The Naranjo score is described in the paper as "a validated tool." The scoring was done by two gastroenterologists evaluating and scoring each case independently from each institution. The Naranjo scale is an accepted tool used by medical researchers to estimate the probability of causal relationship between a drug and an adverse event on the drug. It has been validated since 1981 according to the authors who say "this scale is a causality assessment instrument that is

used to determine the likelihood that a medication resulted in the adverse reaction in question." The Naranjo scale is accepted by Roche itself, and in fact is used by their scientists.

The authors further noted that it has been used in numerous other published articles by medical researchers. The Naranjo scale resulted in a score that classifies each case as highly probable, probable, possible, or doubtful. Roche used the Naranjo scale to assess causality in their own causality reports. The findings were that with a 98% concordance rate between the two independent evaluators it was found that 68% of the cases reviewed were rated as "probable" and an additional 5% were rated as "highly probable."

The authors discussed plausible biological mechanisms by which retinoids could cause IBD including disturbance of "epithelial tissue growth." The authors noted that the "results should be interpreted with caution." They noted, for example, that the nature of adverse event reporting has limitations because of coming from numerous types of sources, but also noted that MedWatch is "a respected source of postmarketing surveillance data." They noted the diagnosis of IBD was based on the available information and that they didn't have the ability to gather additional information; however, they further noted "points were lost if there was no **objective** evidence of IBD." It's the language of the report that created the questions about admissibility. After rating probability of a causal relationship at "probable" or "highly probable" in over 70% of the cases, they said doctors and patients should be "made fully aware of this possible association."

They also noted that "our study is the first systematic examination of this topic." There is no question this article is a learned treatise of type that an expert may rely on and testify about in Court to the jury to support an opinion. The question here is does the fact that the title and the concluding remarks use the term "possible association" mean the study should have been

excluded as evidence. An expert can't take a study and then rely on it to prove something contrary to what it says. In this case, the study itself resulted in findings of "probable" causal relationship. The fact it is the first such study results in the authors expressing themselves in cautious terms and stating additional studies should be done.

The Court found this study was supportive of Dr. Sachar's opinion. It was a properly conducted study done in accordance with accepted scientific methodology and subsequently accepted for publication in a peer reviewed journal. The probable versus possible language is something a jury can understand and evaluate themselves.

Causality Assessments

The causality assessments in issue were internal documents created in the course of defendants' business. When a patient or physician reported an adverse event while using a particular drug, the defendant had its own scientists assess the likelihood of a causal relationship between the adverse event and the use of the drug. During Dr. Sachar's expert testimony, he was allowed to testify about the causality assessments performed by defendants with respect to Accutane. Many of these reports stated that Accutane's association with the reported adverse GI event was "probable" or "highly probable." Roche scientists used this language after their review and assessment. Defendants argue that they were unduly and irreparably prejudiced by the use of causality assessments at trial and that these assessments are not reliable science. This Court found that although the reports are not in and of themselves sufficient to prove causation, the internal assessments of causality by the defendants' own scientists were admissible evidence. In contrast, isolated adverse events themselves are not usually admissible but causality assessments are because they are reports created by defendants' own internal scientists who gathered additional information through an investigation of the adverse event after it was reported,

gathered additional medical information to verify the report and then gave an opinion on causation using the Naranjo scoring scale.

In support of their position against the use of the causality assessments, defendants point to the decision of the Federal Accutane Multi-District Litigation ("MDL") Court to exclude causality assessments from trial. The procedure used by Roche was not presented to Judge Moody according to his decision. One of his reasons for excluding them was the expert didn't know the procedure used by Roche. Evidence on Roche's procedures was placed in evidence in this trial. This evidence supports the use of the assessments.

Before trial this Court had concerns about the use of causality assessments at trial. The defendants initially persuaded the Court that these reports had little more validity than the adverse event reports they were based upon and could not be relied upon by Dr. Sachar in giving his opinion. The Court found even without the causality reports, there was sufficient evidence to support the admission of his opinion. Before the trial began, however, the Court was reconsidering as to how the reports could be used as evidence and advised counsel the final decision would have to await the testimony at trial. In fact, it is difficult to rule *in limine* on evidence questions because the rulings can be changed based on evidence produced at trial.

The defendants argue that there is no question that the causality assessments had nothing to do with an evaluation of causation because Dr. Huber, former Roche Head of Global Safety, testified the purpose of doing causality assessment was not to determine if the drug caused the event. Trial Tr. 2342:23, 2343:1. The Federal decision relied upon by defendant accepted this as true. This was a credibility question. As previously stated, it appears from the decision Judge Moody was apparently not given testimony that explained Roche's procedure for doing the assessment. There was additional testimony presented at trial. The plaintiff had taken the

testimony of Dr. Alan Bess, who had been with Roche from 1986-2000. Before working for Roche he was head of drug safety for Abbott Pharmaceuticals. At Roche, he was U.S. Head of Drug Safety from 1994-2000. Dr. Bess had given testimony at his deposition that was adverse to Roche's positions. At the deposition he was not represented by Roche, and had personal counsel, but at trial he acknowledged meeting with Roche's counsel to prepare for trial and that he no longer had personal counsel.

At trial Dr. Bess' credibility was very much in question because his testimony differed in many instances from his prior testimony at his deposition. As to adverse event reports, he stated the following:

> Q. Tell the jury what a signal is to a drug safety individual, such as yourself.
> A. A signal is a potential trend. It is a side effect. So, if you begin to see several reports of chest pain with a drug, that is a potential signal.
> Q. Okay. Or if you start seeing inflammatory bowel disease, that's a sign or a signal?
> A. Any side effect, it is a potential signal, yes.
> Q. Now, would you agree with me that the more signs and signals there are, the more a pharmaceutical company must begin the process of determining whether those signs an signals are true?
> A. Yes. Trial Tr. 567:19-25, 568:1-6

The witness was then asked about causality assessments and he testified as follows:

> Q. And your company was engaged in a process in which they were making what is referred to as causality assessments, weren't they?
> A. That's correct, yes. ....
> Q. Tell the jury what a causality assessment is.
> A. A causality assessment is an analysis of a particular case, trying to determine whether the event was associated with the drug that was administered. So, what you need to do is look at a number of different factors.
>
> Going back to my previous example of a patient takes a drug and develops chest pain, then it is very important to see whether it was the drug causing it or whether it was other factors. Other factors could have been he had a history of chest pain or he was taking another medication that causes chest pain. We want to see, is there a temporal relationship? Did the chest pain occur at the time the drug was administered?
>
> So, these are -- there's a large number of factors that we look at trying to determine did that drug --was that drug associated with the adverse event.
> Q. Okay. How about this definition, Doctor?

Q. "A causality assessment is a term used in the world of drug safety trying to demonstrate a relationship, a cause and effect relationship, between the drug and an adverse event."

Is that a good definition?

A. That's one way to define it.

Q. Sound like one you gave back when you were under oath?

A. I very well could have. Trial Tr. 569:6-9, 15-25; 570:1-9, 16-24

Dr. Bess in follow-up attempted to explain away his prior statements, but the jury could choose to believe his answer from his deposition that he acknowledged at trial that differs from Dr. Huber's position on the purpose of a causality assessment. Roche's position that the purpose of "causality assessments" was not to evaluate cause and effect was contracted by testimony of its own former employees.

Dr. Reshef, a Hoffmann-Roche employee explained the process used to prepare causality assessments. After getting an adverse inference report, a Roche medical reviewer would review the original report and then contact the patient, doctor, or reporter to fill in missing information. Dr. Reshef would then review them and often send them back for more fact information. After the additional information was obtained the reports were sent to defendants' headquarters in Switzerland where they were evaluated. The report with the additional medical information the company now had was then assessed by a physician at Roche headquarters in Switzerland using the Naranjo scoring scale.

As stated earlier, this way of evaluating "causality" is an accepted and scientifically validated. It is not proof of how X causes Y, nor is it nearly as strong as many other types of studies. Medicine is not an exact science. There is no study or even a well-designed clinical trial that does not have some flaws. People cannot be cut open and examined like animals. They cannot be tested on like animals. Controls are always a problem when studying people. The

legal system does not require certainty, only probability based on what doctors and scientists rely on.

The Court does not find it necessary to delineate the differences between Daubert and Kemp, it is sufficient to hold that under Kemp, Dr. Sachar's testimony, the Reddy article, and the causality assessments, are admissible under New Jersey law. Rule 702 states:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education may testify thereto in the form of an opinion or otherwise. N.J. R. Evid. 702.

Again, the New Jersey Supreme Court has interpreted this rule to mean "a theory of causation that had not yet reached general acceptance in the scientific community may be found to be sufficiently reliable if it is based on a sound, adequately-founded scientific methodology involving data and information of the type reasonably relied on by experts in the scientific field." Kemp, 174 N.J. at 425, citing Rubanick v. Witco Chemical Corp., 125 N.J. 421, 449 (quotations omitted). The evidence doesn't have to be conclusive or irrefutable.

Given the standard set forth in Kemp, it is impossible to consider Dr. Sachar's testimony, the Reddy article, the animal studies or the causality assessments to be "junk science" of the sort both Kemp and Daubert mean to keep out of the Courtroom.

Failure to Test

The jury found defendants liable to plaintiff under a failure to warn cause of action. Because of plaintiff's residence in Alabama at the time of injury and at all other times relevant to the trial, the Court applied the state law of Alabama with regard to a failure to warn claim. Alabama law has long recognized failure to warn causes of action as valid and "the existence of a duty to warn and the adequacy of a warning are questions of fact for the jury." Toole v. McClintock, 99 F.2d 1430, 1433 (11th Cir. 1993) (citing State Farm Fire & Casualty Co. v. J.B.

Plastics, 505 So. 2d 1223, 1227 (Ala. 1987). Further, Alabama law recognizes the "learned intermediary doctrine" whereby "the adequacy of [the warning] is measure by its effect on the *physician*." Toole, 99 F.2d at 1433 (emphasis in original).

Defendants contend that plaintiff improperly argued at trial that defendants had an affirmative duty to test Accutane in the context of its potential relationship to IBD. Defendants argue that due to plaintiff's conduct at trial, the failure to test argument had the effect of improperly shifting the burden of proof from plaintiff to defendants. This argument is founded on the notion that the jury mistakenly believed that defendants could be held liable under a failure to test cause of action, separate and distinct from the failure to warn cause of action. Alabama law does not recognize a separate failure to test cause of action. See McClain v. Metabolife Int'l, Inc., 193 F. Supp. 2d 1252, 1257 (N.D. Ala. 2002) (dismissing plaintiffs' attempt to present a failure to test cause of action and stating "[p]laintiffs have not directed the Court's attention to a single authority supporting the maintenance of such a claim under Alabama law, nor is the Court independently aware of any such authority.").

Defendants cite to authority supporting the nonexistence of a failure to test cause of action, which this Court readily and fully concedes does not exist in Alabama. However, the jury was not instructed that failure to test was a separate cause of action and thus defendants find no support for a judgment notwithstanding the verdict or a new trial. The Court charged the jury as follows:

> A manufacturer has the duty to warn prescribing physicians about potential serious risks of a drug if those risks are known or should be known by the manufacturer.
>
> To be adequate a warning must be the kind of warning which a reasonably prudent manufacturer in the same or similar circumstances would have provided to the prescribing physician. In the case of a prescription drug an adequate warning must be given to the doctors who will prescribe the drug. This is true because it is the prescribing doctor who has to decide whether to prescribe the

> prescription drug to a patient. An adequate warning will communicate sufficient information on the risks of the drug that are known or should be known by the manufacturer. When you consider what's known or should be known you should understand that a reasonably prudent drug manufacturer should be deemed to know of reasonably obtainable and available, reliable information. **The manufacturer of a drug has a duty to take reasonable steps to find out information about the risks of their product, including doing such monitoring, investigation and testing as may be reasonable under the circumstances.**
>
> This duty continues even after the drug is approved and on the market.

Trial. Tr. at 3066:7-3067:6 (emphasis added). The charge given to the jury in the instant case is wholly consistent with the Pattern Jury Instructions approved by the Supreme Court of Alabama:

> A manufacturer of a product which may be reasonably anticipated to be dangerous if defectively made owes a duty to exercise reasonable care in the manufacture of his product so that it will be reasonably safe for its normal uses. **Reasonable care means that degree of care that a reasonably prudent manufacturer of such a product would exercise in the designing, making, inspecting, and testing of the product and the materials and parts of which it is made in order to produce a reasonably safe product.**
>
> The manufacturer of ethical drugs has the duty of making timely and adequate warnings to the medical profession of any dangerous side effects produced by its drugs of which it knows or has reason to know. The manufacturer is directly liable to the patient for the breach of such duty.

Ala. Pattern Jury Instr. Civ. 32.01 (2nd ed.) (emphasis added).

It is clear from the charge given to the jury that there was no separate failure to test claim, however, the jury was able to consider, as a component of failure to warn, what defendants *should have known.* Certainly, the amount of testing done on Accutane is something the jury was permitted to consider in determining what defendants should have known.

Not only were the jury's instructions consistent with the Alabama Pattern Jury Instruction, they were consistent with the state of pharmaceutical products liability law nationally. It is undisputed that pharmaceutical companies have a duty to warn of dangers which it knows or should know. See Lindsay v. Ortho Pharmaceutical Corp., 637 F.2d 87 (2nd Cir.

1980); Golod v. Hoffmann-La Roche, Inc., 964 F. Supp. 841 (S.D.N.Y. 1997). And that that duty encompasses a "continuing obligation" to "keep abreast of knowledge of its product as gained through research, adverse reaction reports, scientific literature and other available methods." Baker v. St. Agnes Hospital, 70 A.D.2d 400, 406 (N.Y. App. Div. 1979). Further, other Courts have upheld similar failure to warn jury instructions in drug liability cases where the charge stated the jury could consider ongoing testing a part of ordinary care. See Young v. Key Pharmaceuticals, Inc., 922 P.2d 59, 68 (Wash. 1996). Thus, the jury instructions on failure to warn were proper and the jury was not misled into considering a separate failure to test cause of action.

It should be clear that the best type of studies on causation were lacking in this case. The "gold standard" that is considered the most scientifically reliable study is a controlled randomized clinical trial.[2] None have been done to examine the causal relationship of Accutane and IBD. The lack of the best evidence is really the foundation of the defense attack on plaintiff's proof in this case. When Dr. Sachar was attacked on the lack of this type of study as a basis for his opinion, he responded in his deposition by attacking Roche saying it was "criminal" the defendant did not do clinical trials in light of their own causality assessments. The Court in a motion *in limine* barred any reference to his belief the failure to test was "criminal." However, the fact that there were no trial done was admissible. Usually it is the manufacturer who tests its product and organizes clinical trials on safety issues. There is something disturbing about defendants' attacking plaintiff's proof because they were unable to produce stronger evidence like clinical trials when the fact is it is the manufacturer who is ordinarily expected to do them but chose not to.

[2] None of this is ever simple in the world of medicine/science. Even when controlled trials are done, esteemed scientists regularly argue over the meaning of the results, the methodology, power of the study, and whether one clinical trial contradicts or supports another.

Exclusion of Evidence

Defendants contend that they were improperly precluded from presenting evidence. Specifically, defendants argue that expert opinion on the number of IBD reports in relation to the number of Accutane users and information on the Food and Drug Administration ("FDA") regulations should have been presented to the jury. Defendants correctly state that "[d]ue process requires that there be an opportunity to present every available defense...." Gonzalez v. Safe & Sound Sec. Corp., 185 N.J. 100, 114 (2005) (citation and quotations omitted). However, to allow defendants to present evidence on the number of Accutane users compared to the background rate of IBD would have presented an unfair suggestion regarding whether a stronger warning was required. As was stated during trial "[t]o suggest that a reasonable company shouldn't explore a rare risk is an unfair suggestion to the jury." Trial Tr. at 2323:1-8. Any calculation based on the number of Accutane users versus the reported number of events would be completely inaccurate. This is true because the number of users is known, but the number of actual adverse events is unknown. The number of reports filed is not the same as the number of events. In fact, events are underreported; for example, Dr. Sachar testified in his entire career he has only filed a few of these reports, and Dr. Reshef also acknowledged that only a fraction of the events are reported. The Reddy article stated that, in fact, only 1% of adverse events may be reported and the authors explained a calculation of the number of users versus the number of reports cannot be used. The number of users might be relevant for other purposes, but it was offered for exactly the wrong purpose to suggest the number of reported events is insignificant compared to the number of users of the drug.

Defendants also argue that they were prejudiced by the Court's exclusion of certain portions of their FDA labeling process evidence. This argument must also fail. Defendants were

not precluded from presenting evidence on the FDA process, rather, they were not allowed to offer evidence attempting to explain away FDA regulations regarding their ability to change Accutane's warning label. Issues of law rather than fact are within the authority of the trial judge. Thus because it was not a question for the jury to interpret the regulations promulgated by the FDA, testimony suggesting the process of changing a warning label is something contrary to a plain reading of the law was inappropriate and unnecessary. Defendants were not entitled to present evidence suggesting they were unable to alter Accutane's warning in any way because this is contrary to the law and regulations.

Evidentiary Support

Defendants argue that there was insufficient evidence to support the jury's finding of liability. Because plaintiff established a prima facie case under Alabama law, it was ultimately a jury question to determine whether or not the warning supplied by defendants was adequate. Thus defendants' argument must fail.

Products liability law in Alabama is governed by the Alabama Extended Manufacturer's Liability Doctrine (AEMLD). See Atkins v. American Motors Corp., 335 So. 2d 134 (Ala. 1976); Casrell v. Altec Industries, Inc., 335 So. 2d 128 (Ala. 1976). The AEMLD provides that "a manufacturer, or supplier, or seller, who markets a product not reasonably safe when applied to its intended use in the usual and customary manner, constitutes negligence as a *matter of law.* Casrell, 335 So. 2d at 132. In terms of pharmaceutical products "the adequacy of the accompanying warning determines whether the drug, as marketed, is defective, or unreasonably dangerous." Stone v. Smith, Kline & French Laboratories, 447 So. 2d 1301 (Ala. 1984). Further, as stated previously, the "adequacy of [the warning] is measure by its effect on the physician" under the "learned intermediary doctrine." Toole, 999 F. 2d at 1433 (11th Cir. 1993).

Most importantly, "the adequacy of a warning [is a question] of fact for the jury." State Farm Fire & Casualty Co. v. J.B. Plastics, 505 So. 2d 1223, 1227 (Ala. 1987).

The jury heard testimony from plaintiff's treating dermatologist Dr. Ann Gerald regarding how she perceived Accutane's warning about its relationship with IBD as well as expert testimony from Dr. Sachar on Accutane and its relationship with IBD. It was ultimately a question for the jury to weigh the testimony and determine if the warning was adequate. It is hardly plausible to suggest that, as a matter of law, no reasonable jury could not have found the warning inadequate when considering the testimonies of Drs. Gerald and Sachar. In fact, other Courts have found that as a matter of law, equivocal warnings such as those employed by Accutane are inadequate. See Thom v. Bristol-Myers Squibb Co., 353 F. 3d 848 (10th Cir. 2003).[3]

Conclusion

Because defendants have failed to make the requisite showings that either "the evidence and uncontradicted testimony [was] plain and so complete that disbelief of the story could not reasonably arise in the rational process of an ordinary intelligent mind" or that there was "clearly and convincingly...a miscarriage of justice," their Motion for Judgment Notwithstanding the Verdict or in the Alternative a New Trial is denied.

CAROL E. HIGBEE, P.J.Cv.

[3] "[T]he package insert for Serzone indicated only that 'rare reports' of pripism were 'temporally associated' with Serzone; it further stated that a 'causal relationship [of priapism] to nefazodone has not been established....' [W]e do not think that this equivocal language is adequate as a matter of law." *Thom*, 353 F. 3d at 853.